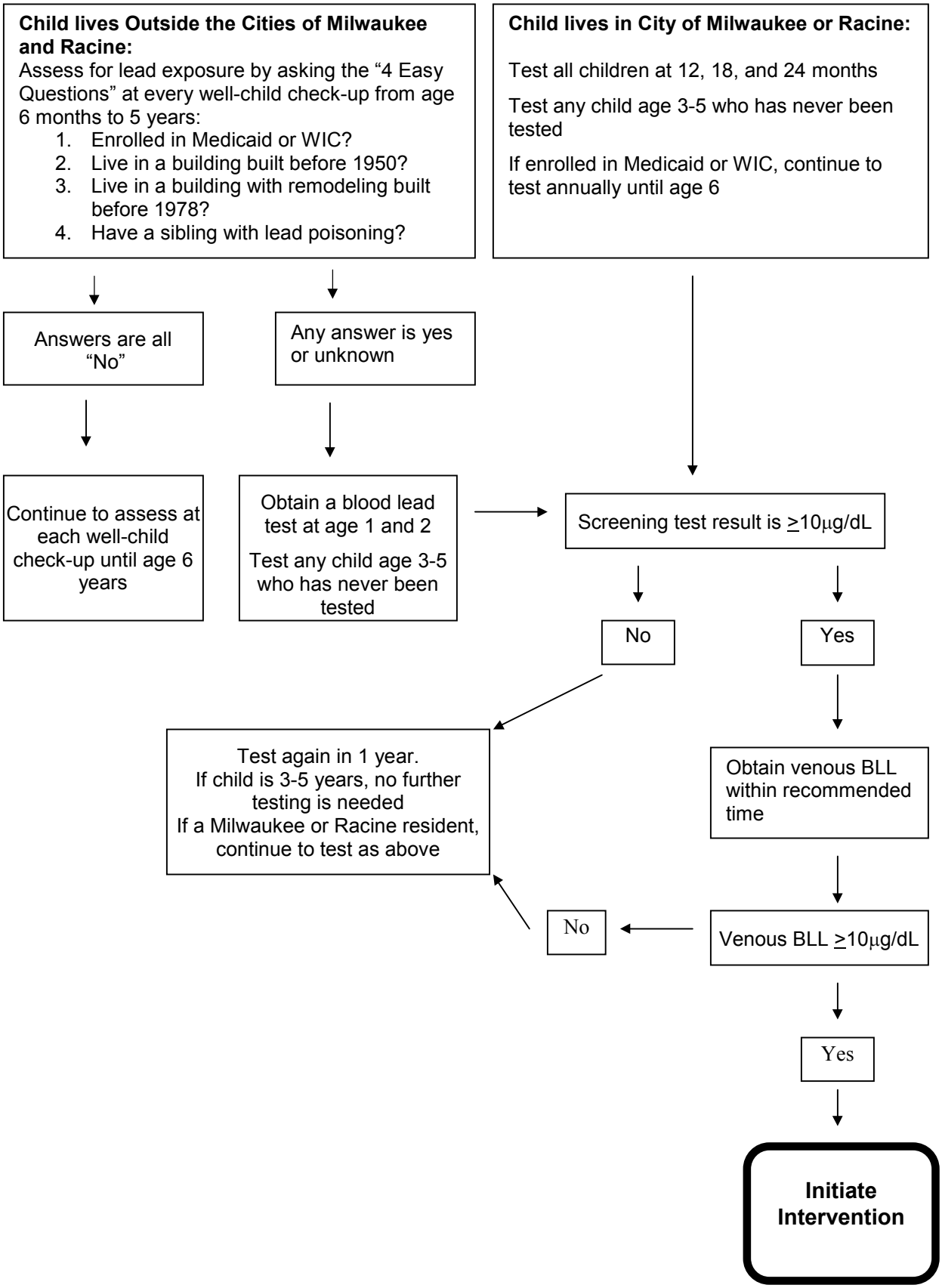
Chapter 7

Screening & Diagnosis of Childhood Lead Poisoning

Content

FLOW CHART: SCREENING WISCONSIN CHILDREN FOR LEAD POISONING



In Brief: A Public Health Blood Lead Screening Program

Goal	Activities
Describe High-Risk Populations in the Community	✓ Identify characteristics of children in the community known to be lead poisoned and the sources of exposure. ✓ Identify locations of children who share these risks ✓ Map blood lead screening tests, lead poisonings, age of housing
Assure Blood Lead Testing is Accessible and Available	✓ List resources (including WIC, HealthCheck, Federally Qualified Health Care Centers, local clinics, community clinics) who provide health care services to identified at-risk populations ✓ Assess barriers to families in obtaining blood lead tests ✓ Establish collaborations to facilitate screening of at-risk children ✓ Identify resources for affordable venous blood lead tests
Monitor Local Blood Lead Testing Practices	✓ Number & percent of children in high risk target populations being screened and those with BLLs $\geq$10μg/dL ✓ Timeliness of venous confirmatory and follow-up tests ✓ Evaluate the referrals of and communication about lead poisoned children between private providers and public health ✓ Work with WCLPPP to obtain provider or site specific screening data to determine screening trends
Provide Information About Blood Lead Testing to Health Care Providers and Parents of Young Children	✓ Assess knowledge of staff at local health care facilities about lead poisoning, screening, follow-up protocols and the health department role. ✓ Develop strategies to provide information on screening to health care staff and to establish effective communication about children with lead poisoning ✓ Develop strategies to effectively communicate to parents of children ages 0-5 about lead exposure and blood lead testing ✓ Identify a desired outcome for educational interventions

Introduction

Screening programs identify persons who have a particular health condition (e.g. lead poisoning) among a group of apparently well people. Without screening programs, persons with adverse health conditions may not be aware of the condition. Usually those with positive results from a screening program require additional diagnostic testing. The results of a screening program should benefit the individual being screened, and benefit the community because earlier detection and treatment of the disease may prevent severe and costly consequences from occurring.

Screening is the strategy used to identify children who are lead poisoned so that appropriate measures can be taken to identify and eliminate lead hazards, and minimize the length of time the child is exposed.

Glossary of Terms

The terminology used to discuss the process of identifying children at risk and providing diagnostic and treatment services can be confusing. Figure 7.1 is a glossary of terms used by the Wisconsin Childhood Lead Poisoning Prevention Program, adapted from CDC.

Wisconsin's Blood Lead Screening Recommendations

In November 1997, The Wisconsin Childhood Lead Poisoning Prevention Program assembled an advisory group of representatives from medicine, public health, WIC, the Wisconsin Medicaid Program, and managed care organizations to develop screening guidelines for Wisconsin. The impetus for this gathering was the release of the revised Federal document, "Screening Young Children for Lead Poisoning" (November 1997), which included the recommendation that each state or local public health agency develop a screening plan that reflects the childhood lead poisoning problem in their area.

Two Unique Screening Schedules

The Wisconsin blood lead screening recommendations are based on an analysis of statewide blood lead test data. When statewide data were analyzed, outside the cities of Milwaukee and Racine there were insufficient numbers of children tested to recommend a single statewide strategy for screening. Therefore, two unique screening schedules make up the Wisconsin Blood Lead Screening Recommendations. These can be found at the end of this chapter and can be reproduced.

Children residing in the cities of Milwaukee and Racine are tested more aggressively than are those residing in other parts of the state. The recommendation is based on a high prevalence of lead-poisoned children, the predominance of pre-1950 rental housing, and a high proportion of children in poverty in those cities. In Milwaukee and Racine, universal screening is recommended for all children at ages 12, 18, and 24 months, and if enrolled in Medicaid, WIC or uninsured, annually at 3, 4, and 5 years of age.[1] Other 3- to 5-year-olds should be tested if they have not been tested previously.

Figure 7.1 GLOSSARY

TERM	DEFINITION
Assessment for Lead Poisoning:	Questions to assess the presence of lead hazards in the child's environment are asked of families at each well-child check-up for children from 6 months through 5 years of age. *No assessment is needed for children enrolled in MA or WIC, two identified high-risk populations. A test should be done at age 1 and 2 years.*
Screening for Lead Poisoning	The routine measurement of blood lead levels (BLLs) in asymptomatic children using a blood lead screening test.
Blood Lead Screening Test	Any test, capillary or venous, for a child who had no previous venous blood lead test result ≥10μg/dL.
Targeted Screening	The blood lead testing of some, but not all children in a defined geographic area based on assessment of the presence of a factor(s) that places them at increased risk for lead exposure.
Universal Screening	The blood lead testing of all children in a defined geographic area at recommended ages (minimally at ages 1 and 2 years, or at age 3-5 years if they have never had a test done before).
Diagnostic Test	A venous blood lead test. If the screening test is venous, it is also a diagnostic test.
Confirmation Test	The first venous test following a capillary screening test ≥10μg/dL. All capillary tests ≥10μg/dL should have a venous confirmation test. The confirmatory test is a diagnostic test. Schedule recommended by CDC:

Capillary screening test result	10-19μg/dL	20-44μg/dL	45-59μg/dL	60-69μg/dL	> 72μg/dL
Obtain confirmatory venous test:	3 months	1 week to 1 month*	48 hours	24 hours	IMMEDIATE

*The higher the screening blood lead level, the more urgent the need for a diagnostic test.

A Follow-up Test

A blood lead test (venous if possible) following a venous BLL ≥10μg/dL. Schedule recommended by CDC:

Venous BLL	10-14μg/dL	15-19μg/dL.	20-24μg/dL.	25-44μg/dL	≥45	
Early Follow-up (first 2-4 tests after diagnosis)	3 months	1-3 months	1-3 months	2 weeks to 1 month	As soon as possible	
Late Follow-up (after BLL begins to decline)	6-9 months	3-6 months	1-3 months	1 month	Per drug protocols	

Lead Poisoned	A child with a blood lead test result ≥10μg/dL is lead poisoned (WI Stat 254.11(9))
Case or Elevated Blood Lead Level	A child with one venous BLL ≥20μg/dL or 2 venous BLLs of ≥15μg/dL at least 90 days apart (WI Chapter 254.11(5m))

Universal screening is applied to children throughout the state who are enrolled in Medicaid. State and federal regulations require a blood lead test at ages 1 and 2 years, and if ages 3 to 5 without a previous blood lead test. The Wisconsin screening recommendations also recommend universal screening at ages 1 and 2 years for children enrolled in WIC.

For children not enrolled in Medicaid or WIC and living outside of the cities of Milwaukee and Racine, targeted screening is recommended. Children will be targeted, or identified at high risk of lead exposure based on assessment questions asked at each well-child check-up from age 6 months to 6 years. The "4 Easy Questions" are asked, and a blood lead screening test is obtained if any response indicates risk of lead exposure. LHDs are encouraged to add additional questions to the basic "4 Easy Questions" if local assessment indicates additional risk factors are present.

Strategies Behind the Wisconsin Screening Recommendations

The Wisconsin Screening Plan recognizes the high risk of lead exposure to Wisconsin children due to the amount of old housing throughout the state. It is rooted in the long-term goal of protecting all children from lead poisoning and eliminating it as the major environmental health threat to children. To that end, early detection and follow-up of lead poisoning among Wisconsin children remains a priority. The screening recommendations reflect four strategies to achieve that end:

1. **Assessment of risk for lead exposure and screening becomes a Pediatric Preventive Care Standard**
   To become a standard of pediatric care, blood lead screening must be viewed as preventive practice within well-child care. Assessing risk for lead exposure during routine pediatric visits for young children should be as common as asking about immunization or car seat use.

2. **The child's environment is considered the primary risk factor**
   The child's environment poses the greatest risk for lead poisoning. Blood lead screening tests are targeted for those children living in high-risk environments.

3. **Children receiving publicly funded health care services are at high risk**
   In many communities, there is a lack of safe affordable housing for low-income families. These families tend to live in housing that is more likely to be rented, older, and poorly maintained. Children who obtain their health care from publicly funded health services such as Medicaid, WIC, and Federally Qualified Health Care Centers do so because the family income is within established criteria for enrollment. Children from these families are at increased risk for lead poisoning, and the focus of screening programs.

4. **Children at Ages 1 and 2 are most vulnerable to lead toxicity**
   Age is the major characteristic of the child that places them at risk for lead poisoning. Blood lead levels are highest for children between the ages 12-36 months. The reasons for increased susceptibility of young children to lead toxicity are best described in this excerpt from Lead Poisoning in Childhood (p. 50):

   > First, at this age, children master ambulation and become capable of exploring all corners of their environment, finding lead sources previously unavailable to them. Second, toddlers receive relatively less parental attention than infants, providing greater opportunity for unsupervised hazardous behaviors. Third, young children, in exploring their environment, often spend a considerable amount of time at the window, a site that tends to have high concentrations of lead, usually in the form of easily absorbed dust. Fourth, toddlers have not only developmentally appropriate

hand-to-mouth activity but also a high rate of pica (i.e., the repeated ingestion of non-food substances). Fifth, toddlers have a high prevalence of iron deficiency, which increases gastrointestinal absorption of ingested lead. Finally, gastrointestinal absorption of ingested lead is inversely related to age. Although adults absorb only 10%-20% of lead, young children absorb 30%-50%

Evaluating a Screening Program

LHDs receiving state general purpose revenue (GPR) funding for lead poisoning prevention activities have a contract with the Department that requires them to establish a blood lead screening program that assures the availability and accessibility of blood lead testing for at risk children. The blood lead screening program may or may not directly collect blood lead samples, but must evaluate whether children at high risk are being tested. The LHD is to perform a systematic review of all blood lead data for incidence, prevalence, and trends in levels of screening and poisoning among target populations, timeliness of diagnostic and other follow-up blood lead tests, and delivery of appropriate services to lead poisoned children.

To evaluate the effectiveness of a blood lead screening program, the following outcome measures can be monitored:

- ✓ Number and percent of children tested by age
- ✓ Positive screening rate (% of those screened with BLLs $\geq$10μg/dL) by age
- ✓ Percent of children enrolled in Medicaid and WIC who were tested
- ✓ Blood lead testing among children residing in pre-1950 housing
- ✓ Timeliness of confirmatory tests for children with elevated capillary screening tests
- ✓ Timeliness of follow-up tests for children with diagnostic BLLs $\geq$10μg/dL

The collection and analysis of this data can be done with the assistance of software programs such as STELLAR, MCH Data System, or DAISy. The STELLAR program, used by WCLPPP, is available free of charge from CDC, and comes with a tutorial. Assistance with the STELLAR program can be obtained from WCLPPP. The DAISy system used by WIC projects can be used to enter blood lead levels, dates screened, and can flag children coming in for certification if they need a blood lead level drawn. The MCH Data System can be used to track children with lead poisoning and the services provided. Screening programs may use the data system that best suits their needs, computerized or paper, as long as it allows them to evaluate their program. The lead program is working with the planners of the public health data system to assure the ability to document lead poisoning prevention activities will be present in SPHERE.

Blood Lead Tests

Testing of whole blood for lead is the screening and diagnostic test of choice to determine lead poisoning, and is the most widely accepted and commonly used measure of lead exposure. A blood lead test is a direct measurement of the concentration of lead in blood. It reflects the dynamic equilibrium between absorption, excretion, and deposition in soft tissue, blood, and bone, and is usually reflective of recent environmental exposure

Venous whole blood lead tests are considered most accurate because of the lower risk of contamination during specimen collection. A single venous blood lead test is considered

diagnostic for lead poisoning. Capillary blood specimens can be utilized for screening purposes with the understanding that a venous diagnostic test is needed to confirm elevated capillary blood lead levels. Because capillary specimens can be easily contaminated, strict attention to protocol must be maintained. Supplies for obtaining blood specimens can be obtained free of charge by calling the Wisconsin State Laboratory of Hygiene (WSLH) at 800-442-4618. The WSLH analyzes both capillary and venous blood specimens. For information on collecting capillary blood lead specimens, see http://www.slh.wisc.edu/ehd/toxicology/procedure.

The efficacy of using filter paper to collect blood lead samples is controversial. The performances of laboratories that analyze the paper, and some collection issues have not been thoroughly investigated. WCLPPP does not endorse the use of filter paper for collecting blood lead test samples and use of filter paper will not be an allowable expense when contracting with DHFS for childhood lead testing. For further information contact Noel Stanton at the Wisconsin State Laboratory of Hygiene (608) 224-6251.

Requirements for Reporting Blood Lead Levels

The statutory requirement for reporting blood lead test results is described in HFS 181 (www.legis.state.wi.us/rsb/code/hfs/hfs181.pdf). All blood lead test results on Wisconsin residents must be reported to the Department of Health and Family Services. The Wisconsin Childhood Lead Poisoning Prevention Program works directly with laboratories to assure reporting of all blood lead tests they analyze. However, the health care providers are accountable for assuring that the complete demographic information required by statute is sent to the laboratory with each blood lead sample.

Erythrocyte Protoporphyrin Tests

Direct measurement of lead in the blood is done by a blood lead test. The blood lead test itself measures only a small proportion of the total body burden of lead. The erythrocyte protoporphyrin (EP) test enhances the interpretation of blood lead test results by providing clues to the total body burden of lead. These tests should be used in tandem to obtain a clear picture of the child's exposure, effectiveness of interventions, and recovery from lead poisoning. An elevated EP test always indicates pathology, and the cause should be evaluated by follow-up diagnostic tests.

What the EP Test Measures

Protoporphyrin is the last precursor in synthesis of heme, the oxygen-carrying component of red blood cells (erythrocytes). Small amounts of protoporphyrin are normally present in erythrocytes, hence the term erythrocyte protoporphyrin. Pathological conditions that impair heme synthesis also cause elevations in EP concentrations. The majority (90%) of EP in the blood is bound to zinc, and is referred to as zinc protoporphyrin. Because the life span of erythrocytes in the blood stream is 90-120 days, the result of an individual EP test reflects the average effect on heme synthesis over 90-120 days. This makes the EP tests an ideal partner with blood lead levels, which can fluctuate over a shorter period of time, to tell the story of lead poisoning.

The terminology associated with EP test results can be confusing. You may see an EP result referred to as erythrocyte protoporphyrin (EP), zinc protoporphyrin (ZP), or free erythrocyte protoporphyrin (FEP). Technically these terms refer to different substances. However, in practice they are often used interchangeably, and test results can generally be interpreted in

identical fashion. The confusion is the result of early methods of laboratory analysis and historical gaps in knowledge about the nature of blood protoporphyrin.

Reporting Units

EP test results are most commonly reported as:

- ✓ μmol EP/mol Heme: molar ratio of protoporphyrin to heme
- ✓ μg EP or ZP/dL Whole Blood: microgram per deciliter whole blood concentration units of EP or ZP

When reported in μg/dL reporting units, EP and ZP results are approximately equivalent. A value exceeding 35μg/dL is widely accepted as indicative of pathology. Resulting exceeding 70μmol/mol are accepted as indicative of pathology. An EP level higher than the threshold value does not indicate the reason for the elevation; further tests for iron deficiency and/or lead poisoning must be performed.

Lead in the blood begins to cause an increase in EP at levels of 15-20μg/dL. As the lead level rises, the EP level rises exponentially. Paired results of EP and BLL can provide information on the effect, extent, and duration of lead exposure. An elevated lead level along with a normal or near-normal EP may indicate that the lead exposure has been recent and/or short term. An elevated EP level, with a minimal increase in BLL may indicate a higher past lead exposure and a continuing body burden of lead. Elevation of both EP and BLL may indicate prolonged and ongoing lead exposure.

Figure 7.3 is an article written by Dr. Margaret Layde, Assistant Professor Medical College of Wisconsin, Downtown Health Center, Milwaukee which describes the use of the EP test in the diagnosis and monitoring of lead poisoning in the clinical setting. The EP test should routinely be obtained on any child with a diagnostic BLL $\geq$20μg/dL, and paired with any follow-up blood lead levels that are drawn.

Iron Deficiency Tests

Iron deficiency can enhance lead absorption and often co-exists with lead poisoning. In addition, research indicates that iron deficiency in young children can exert an independent effect on the central nervous system, as well as enhancing the effects of lead poisoning.

Adequate iron intake lowers lead absorption, and should be considered a primary tool in decreasing the effects of exposure to lead hazards. While the effect of lead on red blood cell production rarely occurs until BLLs reach around 40μg/dL, low iron stores promote absorption of lead at any blood lead level. Over half of US children 1-2 years of age have daily iron intake below recommended amounts. When exposed to lead hazards, these children may suffer lasting effects on cognitive development due to both iron deficiency in infancy and the long lasting negative effects due to lead.

All children with BLLs $\geq$10μg/dL should be evaluated for iron deficiency. Several tests are currently utilized to evaluate iron status. If iron deficiency is diagnosed, supplementation should begin along with treatment of the lead exposure. *Note: Children receiving BAL (dimercaprol) as a chelating agent should not be treated for iron deficiency until the drug therapy is completed.* For more information on nutritional status and lead poisoning, see Chapter 11.

Determining Iron Status

Several tests are used to determine the iron status of a child, but they vary as to their sensitivity and specificity in identifying the cause of iron deficiency.

An EP test is a good screening tool but must be followed by others to determine the exact cause of iron deficiency. An increase in EP is the first biochemical change in erythrocytes due to insufficient iron levels. The advantage of the EP test to measure iron sufficiency is that it reflects iron status in bone marrow, and is more stable than other tests. The disadvantages are that EP is slow to change as a result of dietary iron supplements, and it is non-specific as to the cause of the deficit. Otitis media and respiratory infections in children can cause EP elevations, and are a complicating factor in interpreting test results. EP can also be elevated due to liver disease and malignancy.

Transferrin saturation, or the ratio of serum iron to total iron binding capacity has high specificity, but is subject to contamination with iron and wide diurnal variation. Serum ferritin has high sensitivity and specificity and is often viewed as the most suitable single test to determine iron status. Hematocrit and hemoglobin are crude measures of iron status, reflecting only cases of frank anemia.

Figure 7.3

Usefulness of Erythrocyte Protoporphyrin Tests in Children with Elevated Blood Lead Levels

Written for the Lead Report
by Margaret Layde, MD
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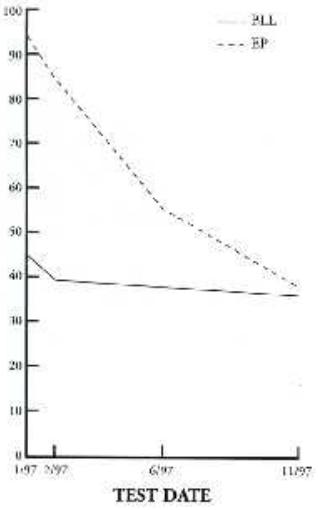
277-8909

A Blood Lead Level (BLL) is the screening test of choice to detect increased lead burdens in children. However, blood lead levels are a poor indicator of the total body burden of lead. With chronic or prolonged lead exposure, the BLL represents only 1-2% of the lead in the body, only the tip of the iceberg. The majority of the lead is in the tissue and the bone.

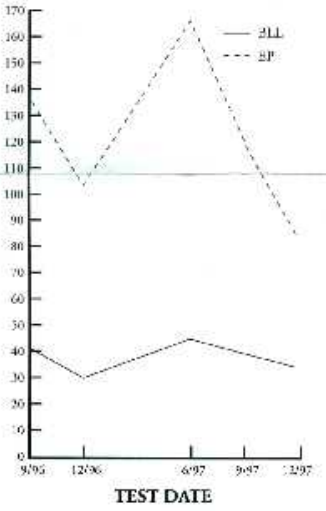
This is where the Erythrocyte Protoporphyrin (EP) levels can provide additional information on body tissue levels. Protoporphyrin is the last precursor in hemoglobin synthesis in the body. Elevated leads of EP reflect impaired heme synthesis, one of the enzymes inhibited by lead. Iron deficiency and hemolytic anemia will also cause an elevated EP, so these must be ruled out.

Although EP is not as sensitive as a screening tool for lead exposure, it helps measure the effects of lead on the body tissues. At the present time we do not have a better way to measure the total body burden of lead. For example, a child with a BLL of 33 and an EP of 200 has a much higher total body burden of lead than a child with a BLL of 33 and an EP of 80 or 40. The higher the EP, the more persistent the BLL elevations will be, provided we have ruled out iron deficiency.

The half-life of lead in the body is very long. Most of it is bound to the bone, but it is in a steady state of equilibrium with the blood lead. It can be very frustrating to monitor the slow decreases in BLL in a child previously exposed to lead. The EP levels more accurately reflect the progress in decreasing the lead burden in the body tissue. In this example, one three-year-old boy was monitored every 2 to 4 weeks for 6 months. His BLL remained high, but his EP showed the effects of chelation and removing lead hazards:



Post-chelation is another time when following both the EP and BLL can be useful. We expect the BLL to decrease dramatically and then rebound in the month or two following chelation, as the bone lead reequilibriates with the blood lead. The blood lead often will return to around 70% of the prechelation level. It can be difficult to know if the child continues to be exposed to lead without also monitoring the EP. The EP should continue to decrease unless there is a new exposure. For example, this girl was reexposed to lead hazards between December 1996 and June 1997.



In summary, Erythrocyte Protoporphyrin levels are a useful adjunct in monitoring children with BLL over 20 micrograms per deciliter. EP indicates the extent of the total body burden of lead and is useful post-chelation to follow progress in decreasing the total body lead burden and ensuring no new lead exposure.

WISCONSIN BLOOD LEAD SCREENING RECOMMENDATIONS

Ask each family the "4 Easy Questions" at each well-child visit between the ages of 6 months through 5 years. A clinic site that serves many children who are enrolled in Medicaid or WIC, are uninsured or underinsured may choose not to ask the "4 Easy Questions" and simply obtain a blood lead test on all children at the recommended ages (see below). If a child that does not routinely receive preventive health care is seen for any reason at a clinic site, include an assessment for lead and immunization status and provide needed services.	"4 Easy Questions": 1. Does the child now live in or visit a house or building built before 1950? Have they ever in the past? (include places such as day care, home of friends, grandparents or other relatives)? **Answer of "yes" or "don't know" indicates risk of exposure**. 2. Does the child now live in or visit a house or building built before 1978 with recent or ongoing renovations? Have they lived in such a building in the past (include places such as day care, home of friends, grandparents or other relatives)? **Answer of "yes" or "don't know" indicates risk of exposure.** 3. Does the child have a brother, sister, or playmate who has been diagnosed with lead poisoning? **Answer of "yes" indicates risk of exposure.** 4. Is the child enrolled in (or eligible for) Medicaid or WIC? **Answer of "yes" indicates risk of exposure. State and federal Medicaid policies require lead testing of all Medicaid children at around ages 12 and 24 months and between 36-72 months if no previous test documented.**
Obtain a blood lead test at ages 1 and 2 years	✓ If any answer to the 4 Easy Questions indicates a risk of exposure
Obtain a blood lead test if at ages 12, 18, & 24 months	✓ If the child lives in the city of Milwaukee or Racine.
Obtain a blood lead test from a child between the ages of 3-5 years with no documented blood lead test	✓ If any answer to the 4 Easy Questions indicates a risk of exposure ✓ If the child is enrolled in Medicaid or WIC
Obtain a blood lead test annually from a child at ages 3, 4, and 5 years:	✓ If the child is enrolled in Medicaid, WIC, or is uninsured and lives in the cities of Milwaukee or Racine

Source: "A Wisconsin Physician's Guide to Blood Lead Screening & Treatment of Lead Poisoning in Children", November, 2000

References

Lead Exposure Associated with Renovation and Remodeling Activities: Wisconsin Childhood Blood Lead Study, United States Environmental Protection Agency, March, 1999

A Wisconsin Physician's Guide to Blood Lead Screening & Treatment of Lead Poisoning in Children, Wisconsin Department of Health and Family Services, October, 2000.

Lead Poisoning: Federal Health Care Programs Are Not Effectively Reaching At-Risk Children, U. S. General Accounting Office, January, 1999.

Pueschel,S., Linakis, J, Anderson, A., *Lead Poisoning In Childhood,* Paul H. Brookes Publishing, Baltimore, MD, 1996

Schlenker, T., Fritz, C., Mark, D., Layde, M., Linke, G., Murphy, A., Matte, T., "Screening for Pediatric Lead Poisoning." *JAMA* 271,1994, pp. 1346-1348.

Stanton, Noel V., "Erythrocyte Protoporphyrin", *Therapeutic Drug Monitoring and Toxicology,* American Association for Clinical Chemistry, Inc., 2000

Valanis, B. *Epidemiology in Nursing and Health Care*. Norwalk, CT: Appleton-Century-Crofts, 1986.

Weitzman, M. and Glotzer, D. "Lead Poisoning." *Pediatrics in Review* 13 (12), December 1992, pp. 461-468.

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